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Cellular Microvesicles in the Blood of Patients with Systemic Lupus Erythematosus

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Abstract
Systemic lupus erythematosus (SLE) is an autoimmune disease with a complex and largely unclear pathogenesis. Cellular phospholipid microvesicles released upon activation and/or death of a cell have been proposed to play a role in inflammatory autoimmune pathologies, including SLE. Here, circulating microvesicles of various cellular origins were marked with fluorescently labeled cell-specific antibodies and enumerated by flow cytometry in platelet-free plasma obtained from the heparinized blood of 29 SLE patients and 19 normal subjects. Significantly higher concentrations of endothelial-, monocyte-, and erythrocyte-derived microvesicles were found in the SLE patients compared to normal subjects with prevalence of microvesicles originating from endothelial cells. No significant difference was found for platelet-derived microvesicles. A correlation analysis of microvesicle counts with laboratory parameters and clinical features of SLE suggest differential implications of various cell-derived microvesicles in the pathogenesis of SLE. These data suggest that SLE is associated with functional alterations of endotheliocytes, monocytes, and erythrocytes followed by enhanced release of microvesicles that may contribute to inflammation and hypercoagulability.

Keywords Microvesicles · Systemic lupus erythematosus · Flow cytometry

1 Introduction

Microvesicles (MVs) are a heterogeneous population of phospholipid vesicles up to about 1 μm in size released from various cells, including blood cells and endothelium, in response to cell activation, aging, and apoptosis [1]. Circulating MVs can play an important physiological role in normal conditions [2, 3] as well as in inflammation, cancer, angiogenesis, thrombosis, etc. [4]. The blood levels of cell-derived circulating MVs of various origins are often increased compared to healthy subjects and MVs contribute to the pathogenesis of various diseases, including inflammatory and autoimmune pathologies [5].

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that affects multiple tissues and organs, leading to relatively high morbidity and mortality rates [6]. The pathogenesis of SLE is complicated and, despite numerous studies, remains largely unclear [7]. The role of MVs in the mechanisms of SLE has been a matter of controversy. Some studies reported elevated levels of circulating MVs in SLE [8], while others found that the number of MVs in the blood is either unchanged or even decreased [9]. The cellular origin of circulating MVs as well as their functional importance in SLE remains vague, although potentially, the content and cellular origins of circulating MVs may shed light on the pathogenesis of SLE and serve as biomarkers of disease activity and progression.

The aim of this study was to determine the levels of cell-derived circulating MVs in SLE patients with respect to their origin and reveal associations between clinical features and the levels of circulating MVs.

2 Materials and Methods

2.1 SLE Patients and Healthy Subjects

The study was approved by the Ethical Committee of Kazan State Medical Academy (Kazan, Russian Federation) and performed in accordance with the Declaration of Helsinki. Patients with SLE enrolled in this study were from the

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